

Figure 1. Energy storage metabolite content of a *Drosophila PRL-1* mutant

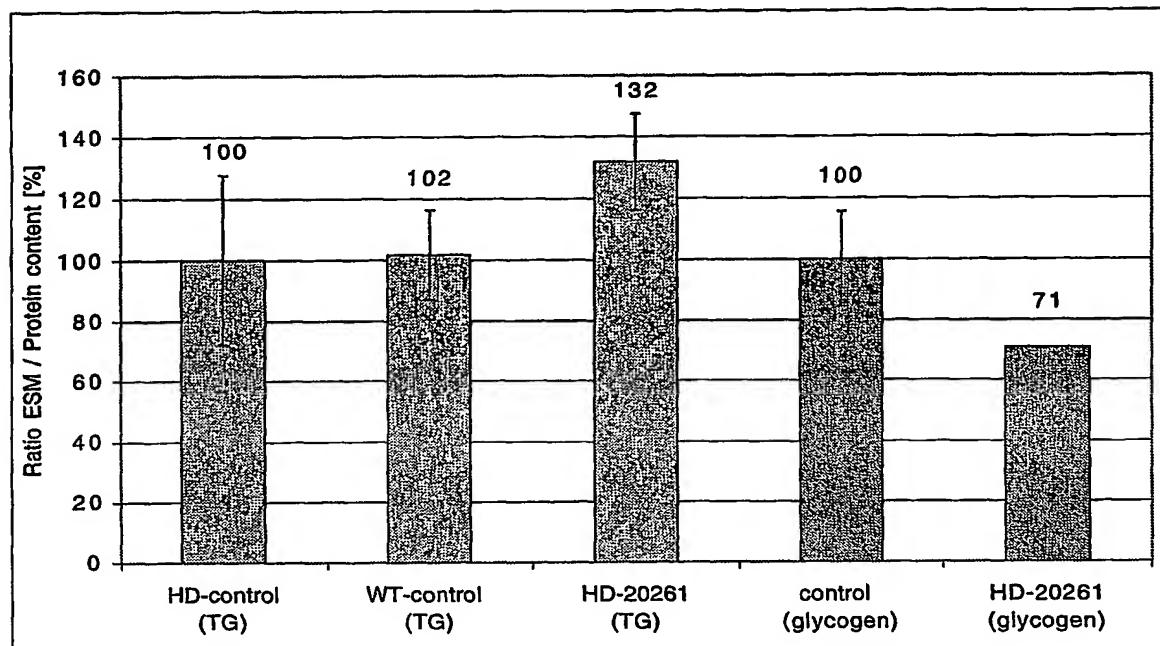


Figure 2. Molecular organization of the *PRL-1* gene (GadFly Accession Number CG4993)

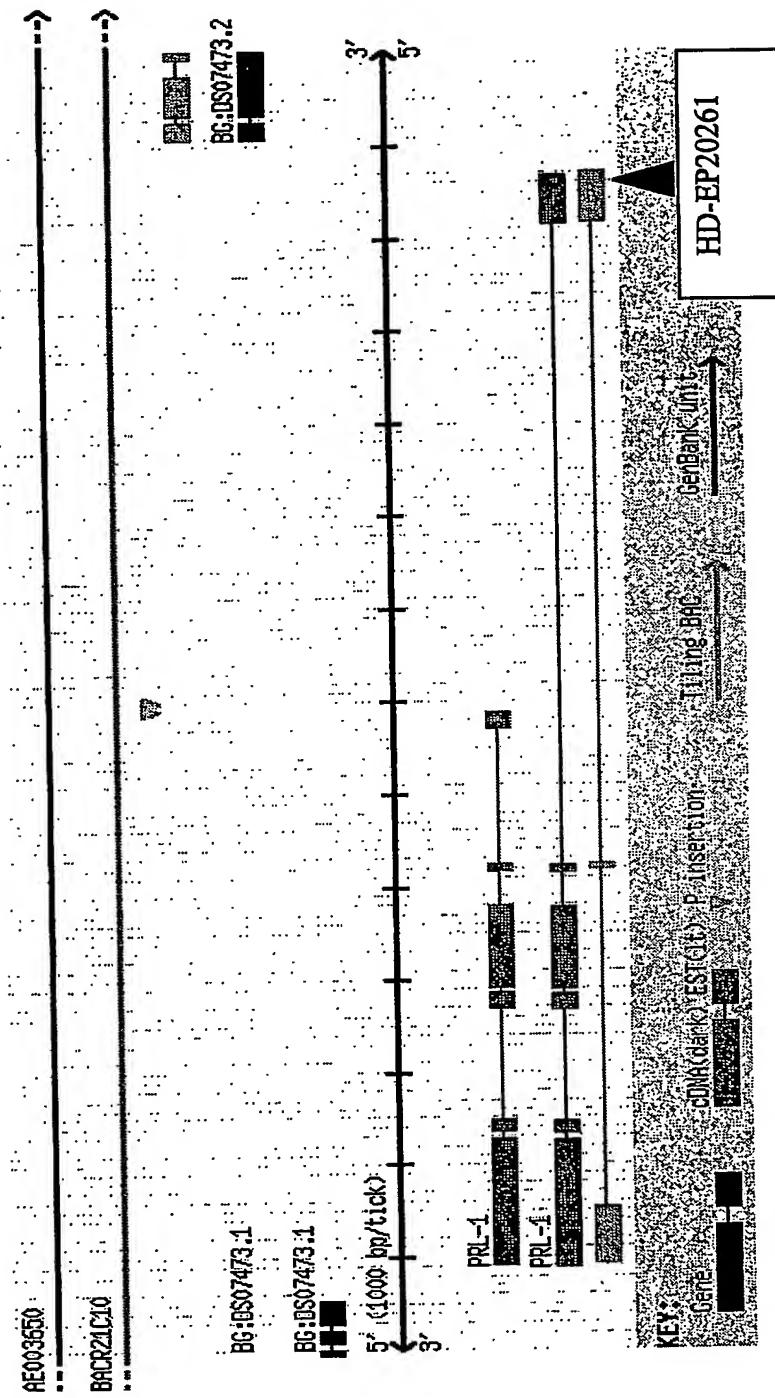


Figure 3. Nucleic acid sequences encoding the human proteins of the invention and amino acid sequences of the proteins of the invention

Figure 3A. *Homo sapiens* protein tyrosine phosphatase type IVA, member 1 (Prl-1), Nucleic acid sequence (SEQ ID NO: 1)

1 cccggctcggt acgcgcgtcg ctccgagccg ctaactgcgt ggttagagtc ggtccccccg
61 ccgtcgccctg catcgccgccc accggccgctc cgccacgacc accgcccgcct cctgcccctgc
121 agccaccgccc accgcctgtg tcgcccgcgc ctgggaccg gctgtatgat taggcacaa
181 ttttcaatgat gtaaacatata tcctcaattc tgggtgttcc ttggtcacac atttatggag
241 tttctgaagg gcagtgagaa ttactgcag gcacagcagc acctctatgc agacaagtgt
301 actgtagaaa ctgattactg ctccaccaag aagccccat aagagtggtt atcctggaca
361 cagaagtgtt gaattgaaat ccacagagca ttttacaaga gttctgaccc gatggggta
421 aacctcagtg cacttcttt ctgtggcct cagtattact ggattgaaga attgctgc
481 cttgttagga gttcatttc acttatacatt acttacaact tcataactcaa agcactgaga
541 atttcaagtg gagtatattg aagtagactt cagttctt gcatcatttc tttttcaat
601 ttttttaattt atttcataac cctattgagt gtttttaac taaattaaca tggctcgaat
661 gaaccgccccca gtcctgtgg aagtcacata caagaacatg agattctt ttagacacaaa
721 tccaaaccaat ggcacccctaa caacttatga cactactt atgatggtgc accccatcc
781 aatagtaaga gtatgtgaag agttcgtga agaacctggt ttttttattt agaggaactt
841 tggcttgcatt tggccttttgc aacccatcc aaccagattt tgatgactg
901 gttaaatgtt gtgaaaatattt ctccagttact tggccctta gcattaattt aaggtggat
961 cgttgcaggc cttgggagag aattcataag aaaaaagcgg cgtggagctt ttaacagca
1021 gaaatacggaa gatgcagttac agtacgtcc taaaatgcgg ctgcgttca aagattccaa
1081 gcaacttctg tattttggaga gcattcaata aaattggggt gcctaattgt actggaaatgt
1141 cggtcataaga aacaactgtt tttgttatac atattagccaa acatgttggc ttagtaagt
1201 gaacttgaga tagggcctaa tatttttttgc ttttttttttgc ttttttttttgc
1261 taatgaagct tccataggag ttttttttttgc ttttttttttgc ttttttttttgc
1321 ttggcaacct ctgttattttgg ttttttttttgc ttttttttttgc ttttttttttgc
1381 gctgtcagca tataaaatgt ttttttttttgc ttttttttttgc ttttttttttgc
1441 agtatttgagt tatgacttgtt ttttttttttgc ttttttttttgc ttttttttttgc
1501 aatttttaggaa gatttaggtgc ttttttttttgc ttttttttttgc ttttttttttgc
1561 acagaagtaa aatcccagga ttttttttttgc ttttttttttgc ttttttttttgc
1621 atttcaaaaca ttgaaaatgtt ggcctacatg gtatttttgc tgctactt atgttacat
1681 ctccccacatt cataccaaata ttttttttttgc ttttttttttgc ttttttttttgc
1741 accaagtctt acagtgttatttttttttgc ttttttttttgc ttttttttttgc
1801 aaaaacctcc attttggaaa ttttttttttgc ttttttttttgc ttttttttttgc
1861 caaaaaaaagcc ttacattat ttttttttttgc ttttttttttgc ttttttttttgc
1921 ctgagaaaaag aatggggaggg ttttttttttgc ttttttttttgc ttttttttttgc
1981 gtgcaaaatcat gttagaatatgt ttttttttttgc ttttttttttgc ttttttttttgc
2041 gctttttgtt ttttttttttgc ttttttttttgc ttttttttttgc ttttttttttgc
2101 agaaatgtgt ttaccaactt ttttttttttgc ttttttttttgc ttttttttttgc
2161 ctcttttgc aaaaaagaaaa ttttttttttgc ttttttttttgc ttttttttttgc
2221 atgccttttgc gagctgtgt ttttttttttgc ttttttttttgc ttttttttttgc
2281 ttgataaaat ggtgtgtt ttttttttttgc ttttttttttgc ttttttttttgc
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2641 ttatataactt tttaaagggtc ttttttttttgc ttttttttttgc ttttttttttgc
2701 aaataatgtt tagtagagga ttttttttttgc ttttttttttgc ttttttttttgc
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2941 aatttttttttgc gaatagcagt ttttttttttgc ttttttttttgc ttttttttttgc
3001 ctccaccccttgc ttttttttttgc ttttttttttgc ttttttttttgc ttttttttttgc

3061 tatttcattg gatttttagac agggcaaaaag gaagaacagg ggcctctgga ggcccttggg
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 3181 aggtttgtt ttttttttaa agggaaatgca gccttagtctt gagaacataa ttttatataa
 3241 tcaattacta aatgttaaac tattaccaca cagcccataa aacagcattt gcgttattg
 3301 agagagagga tttgtccatca tgattaatgtaa aactatctt ttgagtttga aaagaatta
 3361 atttgcagtg tttggattgt atatatggtg ctaaaaataa attaatttac ttatataaacc
 3421 ttatctgtac attatacgtat gtgtatgaaat ttgtatcttg
 3481 taaaatatggc taattataagg aatgcctata atacatctta gattccttat atctaataag
 3541 agttcaaaaga gttatgagtt gaagtcttga atgcagaaa ctatctgata gtgttctaaa
 3601 atttggttac ttgggttgg atacccttag tgggatgatg taaatagagg ctagtaccc
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 3721 aatgccatct ctttttagtt gaaggaaaac tctggaaagta ggtgccattt gtcattctgc
 3781 agtgcactgc aaccattgtt tcccttagtgc ccccttttc cctagggcat tgctctccta
 3841 ttcccacgccc ttaacacacgc tctataccta gaagcagcca gcccaggcat gcagtcacat
 3901 ttaatcacat ccccccttcta gagtgcttca aaatgtatgtat gtcctcaac ttggctaaag
 3961 aatctcaatc tcttggaaatt tatttttttta atgtcatatt catctggtaa atatctactg
 4021 tttgccaggc atttaagaat atgccaaga acataaaaga tgggtgtcacc agattttgg
 4081 caccaatgag tacccgaccc gttgccatga ttaagagaga atgctttcta ttggagttt
 4141 aggaaatata atttggaaat actttaaagg gaagtggaaat tataagtggaa tgatatttt
 4201 cttttacatg taaacaatgtaa agttatgttca aagttaaatgtt ttaaaacaaaa tacatgtt
 4261 agtgtctgccc atacatgttta atattctaca ttcttgcttc cttttttttttaa tatgtttgt
 4321 tgttatatatg tgcctcacac ctgaattgaa aattaaagac tggttttttttttaa gtggttaaaa
 4381 aaaaaaaaaaaa aaaa

Figure 3B. Homo sapiens protein tyrosine phosphatase type IVA, member 1 (Prl-1), Amino acid sequence (SEQ ID NO: 2)

1 marmnlpapv evtyknmrfl ithnptnatl nkfieelkky gvttivrvce atydttlvek
 61 egihvldwpf ddgappsnqi vddwlslvki kfreepgcci avhcvaglgr apvlvalali
 121 eggmkvedav qfirqkrrga fnskqllyle kyrpkmlrf kdsnghrnmc ciq

Figure 3C. Homo sapiens protein tyrosine phosphatase type IVA, member 2 (Prl-2), Nucleic acid sequence, transcript variant 1 (SEQ ID NO: 3)

1 agccccggctg cgcgaagtca tcgctgttcc agacagcgat gactcgagag cgggtgggggt
 61 ggccggcgca tcggccgggc tggtaaccgtc gtctgtccgg gagcggctgg agcggcagcg
 121 gccggccggc acggcgcgag gtgacgccc acggcagcgg cggcagcgg ggcagcggcg
 181 gcagcaggag acgcagcggc gcccgcagca gcagcagcaa gacggactcg tggagacgcg
 241 cccggccggc cggccggccgg cggggccggg tggcgccgc cgaggctggg ggggagtcgt
 301 cggccggccgc gccaccgcgta cggccggccgc cggccggccg gaggtgactg aggagagagg
 361 cgcctctcg ctccccccac cggccggactt caatccccag tccccagctc gcccggctt
 421 ttcgttggaa tatacgttgc acattttatgg cgattctgag tggatggggca gacttctgccc
 481 aggttcagca cagcatttc gctgacaatgtt gagctggag gttctatgtt ccataattaa
 541 cattgccttg aagactcctg gacaccgaga ctggcctcag aatagttgg cttttttttt
 601 ttttaattt caagcatatt tcttttaatg actccagtaa attaagcat caagtaaaca
 661 agtggaaatg gacctacact ttaactttt ctcacttagtgc cttttttttttaatgtt gtaaaggctg
 721 cttaagttttt gttatgtatgtt ggatttttt ggttccatctt gcaatggat atttccatct
 781 agggccaaat tgaatttggaa ttcaagtggaa ttcttaataatc ttgttcttatac ttgaagagag
 841 aagtttcata aggaataaaac aagttgaata gagaaaacac tgattgataa taggcatttt
 901 agtggctttt ttaatgtttt ctgtgtgaa acattcaag atttattgtt tttttttttt
 961 cactttcccccc atcacactca cacgcacgc cacaactttt atttgcctata atgaaccgtc
 1021 cagccccctgt ggagatctcc tatgagaaca tgcgtttct gataactcac aaccctacca
 1081 atgctactct caacaagtcc acagaggaac ttaagaagta tggagtgacg actttggttc
 1141 gagtttggaa tgctacatata gataaagctc cagttggaaa agaaggaatc cacgttctag
 1201 attggccattt tggatgtggaa gctccacccccc ctaatcagat agtagatgtat tggttaaacc

Figure 3D. *Homo sapiens* protein tyrosine phosphatase type IVA, member 2 (Pr1-2), Amino acid sequence transcript variant 1 (SEQ ID NO: 4)

1 mnnpapveis yenmrflith nptnatlnkf teelkkygvt tlrvrcdaty dkapvekegi
61 hvldwpfdg apppnqivdd wlnllktkfr eepgcccavah cvaglgrapv lvalaliecg
121 mkvedavgfi rkrrrgafns kgllylekyr pkmrllfrdt nghccvq

Figure 3E. Homo sapiens protein tyrosine phosphatase type IVA, member 2 (Prl-2), Nucleic acid sequence, transcript variant 2 (SEQ ID NO: 5)

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1 agcggggctg cgcgaagtca tcgctgttcc agacagcgat gactcgagag cggtgggggt
61 ggcggcgcga tcggccgggc tgtaaccgtc gtctgtccgg gagcggctgg agcggcagcg
121 gcggccgggc acggcgcgag gtgacgcccac agggcagcgg cggcagcggaa ggcagcggcg
181 gcagcaggag acgcagcggc ggccgcagca gcagcagcaa gacggactcg tggagacgcg
241 cgcgcgcgc cgcgcgcggg ccggccggg tgctgcgcgc cgaggctggg ggggagtcgt
301 cgcgcgcgc cgcaccgcgtc cgcgcgcgc cgcgcgcgc gagggtactg aggagagagg
361 cgcctcctcg ctccccgcac cgcggactt caatgcggactt tccccagctc gccagcgtt
421 ttctgtggaa tatacgttgc acatttatgg cgattctgag tttgaggggca gacttctgcc
481 aggctcagca cagcatttc gctgacaagt gagcttggag gttctatgtt ccataattaa
541 cattgccttg aagactcctg gacaccgaga ctggcctcag aaatagttgg cttttttttt
601 ttttaatttcaaggat ttttttttttactccatggaa ttttttttttactccatggaa aatataagcat caagtaaaaca
661 agtggaaagt gacctacact ttttttttttactccatggaa ttttttttttactccatggaa gtttttttttactccatggaa aatataagcat caagtaaaaca
721 cttaagttttt gtagttagttt ggattttttggatccatggaa ttttttttttactccatggaa aatataagcat caagtaaaaca
781 aggcccaaat tgaatttttggatccatggaa ttttttttttactccatggaa aatataagcat caagtaaaaca
841 aagtttcata aggaataaaac aagtttggatccatggaa ttttttttttactccatggaa aatataagcat caagtaaaaca
901 agtggtctttt ttaatgtttt ctgtgtgaa acatttcaag atttattgtt ttttttttttactccatggaa aatataagcat caagtaaaaca
961 cacttttttttactccatggaa ttttttttttactccatggaa aatataagcat caagtaaaaca
1021 cagccctgtt ggagatcttcc ttttttttttactccatggaa aatataagcat caagtaaaaca
1081 atgttacttcc ttttttttttactccatggaa aatataagcat caagtaaaaca
1141 gagtttggatccatggaa ttttttttttactccatggaa aatataagcat caagtaaaaca
1201 attggccattt ttttttttttactccatggaa aatataagcat caagtaaaaca
1261 ttttttttttactccatggaa aatataagcat caagtaaaaca
1321 gtttttttttactccatggaa aatataagcat caagtaaaaca
1381 aagatgcagt ttttttttttactccatggaa aatataagcat caagtaaaaca
1441 ttttttttttactccatggaa aatataagcat caagtaaaaca
1501 gtttttttttactccatggaa aatataagcat caagtaaaaca
1561 acttttttttactccatggaa aatataagcat caagtaaaaca
1621 atttttttttactccatggaa aatataagcat caagtaaaaca
1681 ttttttttttactccatggaa aatataagcat caagtaaaaca
1741 aaggatgatt ttttttttttactccatggaa aatataagcat caagtaaaaca
1801 aatccctgtt ttttttttttactccatggaa aatataagcat caagtaaaaca
1861 aggcttgc ttttttttttactccatggaa aatataagcat caagtaaaaca
1921 ttttttttttactccatggaa aatataagcat caagtaaaaca
1981 tccttccttctt ttttttttttactccatggaa aatataagcat caagtaaaaca
2041 ttgttgcgtt ttttttttttactccatggaa aatataagcat caagtaaaaca

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Figure 3F. Homo sapiens protein tyrosine phosphatase type IVA, member 2 (Prl-2), Amino acid sequence transcript variant 2 (SEQ ID NO: 6)

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1 mnrpapveis yenmrflith nptnatlnkf teelkkygvt tlrvcdaty dkapvekegi
61 hvldwpfddg apppnqivdd wlnnlktkfr eepgcvavh cvaglgrapv lvalaliecg
121 mkyedavqfi rqkrrgafns kqllylekyr pkmrlrfrdt nghccvq

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Figure 3G. Homo sapiens protein tyrosine phosphatase type IVA, member 2 (Prl-2), Nucleic acid sequence, transcript variant 3 (SEQ ID NO: 7)

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1 agcggggctg cgcgaagtca tcgctgttcc agacagcgat gactcgagag cggtgggggt
61 ggcggcgcga tcggccgggc tgtaaccgtc gtctgtccgg gagcggctgg agcggcagcg
121 gcggccgggc acggcgcgag gtgacgcccac agggcagcgg cggcagcggaa ggcagcggcg
181 gcagcaggag acgcagcggc ggccgcagca gcagcagcaa gacggactcg tggagacgcg

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241 ccggccgcccgc cgccgccccggg ccggggccggg tgtcgcgcgc cgaggctggg ggggagtcgt
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 481 aggctcagca cagcatttc gctgacaagt gagcttggag gttctatgtt ccataattaa
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 601 ttttaatttgc caagcatatt tcttttaatgc actccagtaa aattaagcat caagtaaaca
 661 agtggaaaatgc gacccatact tttaacttgc ttcactagtgc cctaaatgtt gtaaaggctg
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 901 agtggcttttgc ttaatgttttgc ctgtgtgaa acatttcaag atttattgtt tttttttttt
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 1621 aaaataggcatttgc tctaaggaaa accaggcata cattaggcatttgc gtcggaaaacc atctgttttgc
 1681 ggagcacacttgc

Figure 3H. Homo sapiens protein tyrosine phosphatase type IVA, member 2 (Prl-2), Amino acid sequence, transcript variant 3 (SEQ ID NO: 8)

1 mnrpapveis yenmrflith nptnatlnkf teelkkygvt tlrvrcdaty dkapvekegi
 61 hvlkkkgsqfqtaalfgei pt

Figure 3I. Homo sapiens protein tyrosine phosphatase type IVA, member 3 (Prl-3), Nucleic acid sequence (SEQ ID NO: 9)

1 tgactatcca gctctgagag acggggagttt ggagttgccc gctttactttt ggttgggttg
 61 gggggggccgg cgggctgtttt tggccctttt cttttttaag agttgggttt tcttttttaa
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 541 gtttgcgttgc gggccggcccccc cggccggccaa ggtatgttgc gactggcttgc gcctgggt
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 661 cccggcgttgc tggccatgttgc cggccgttgc tatttgcata gggatgttgc acgaggacgc
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1201 ttttgtaacc actggggcccc cagccccctct tttgcgaccc cttgtcctga cctgttctcg
1261 gcaccttaaaa ttatttagacc ccggggcagt caggtgctcc ggacacccga aggcaataaaa
1321 acaggagccg tgaaaaaaaaaaa aaaaaaaaaaaa aaaaaaaaaaaa aaaaaaaaaaaa
1381 aaaaaaaaaaaa aaaaaaa

Figure 3J. Homo sapiens protein tyrosine phosphatase type IVA, member 3 (Prl-3), Amino acid sequence (SEQ ID NO: 10)

1 marmnlpapv evsykhmrfl ithnptnatl stfiedlkky gattvvrvc vtydktpmek
61 dgitvvvdwpf ddgapppgkv vedwlslvka kfceapgscv avhcvaglgr apvlvalali
121 esgmkyedai qfirqkrrga inskqltyle kyrpkqrlrf kdphthktrc cvm

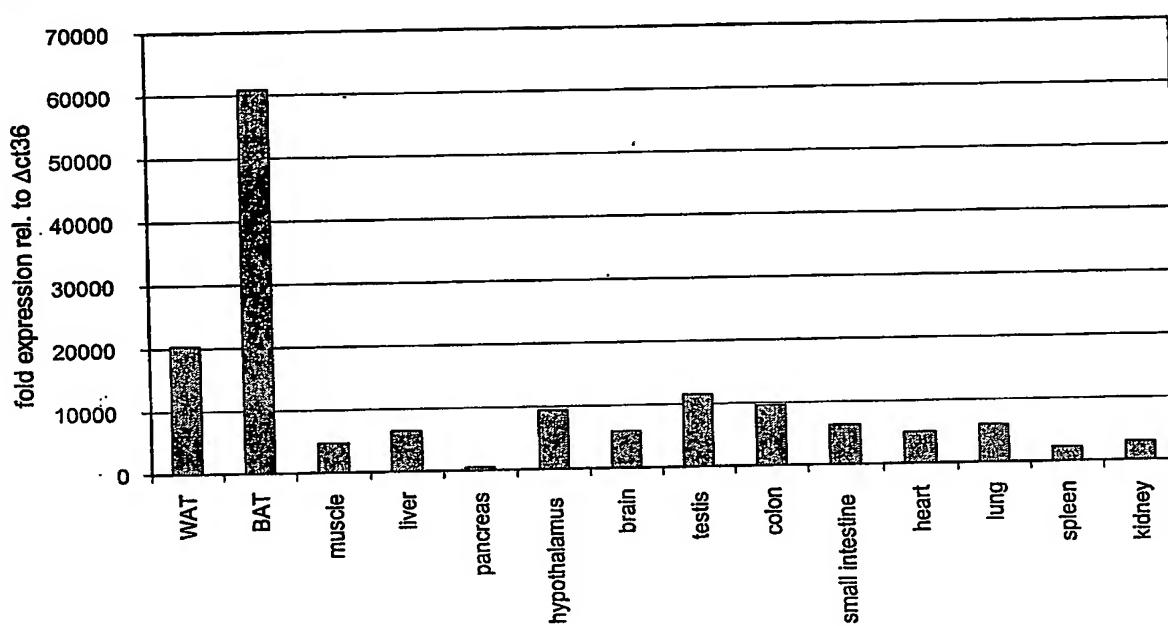
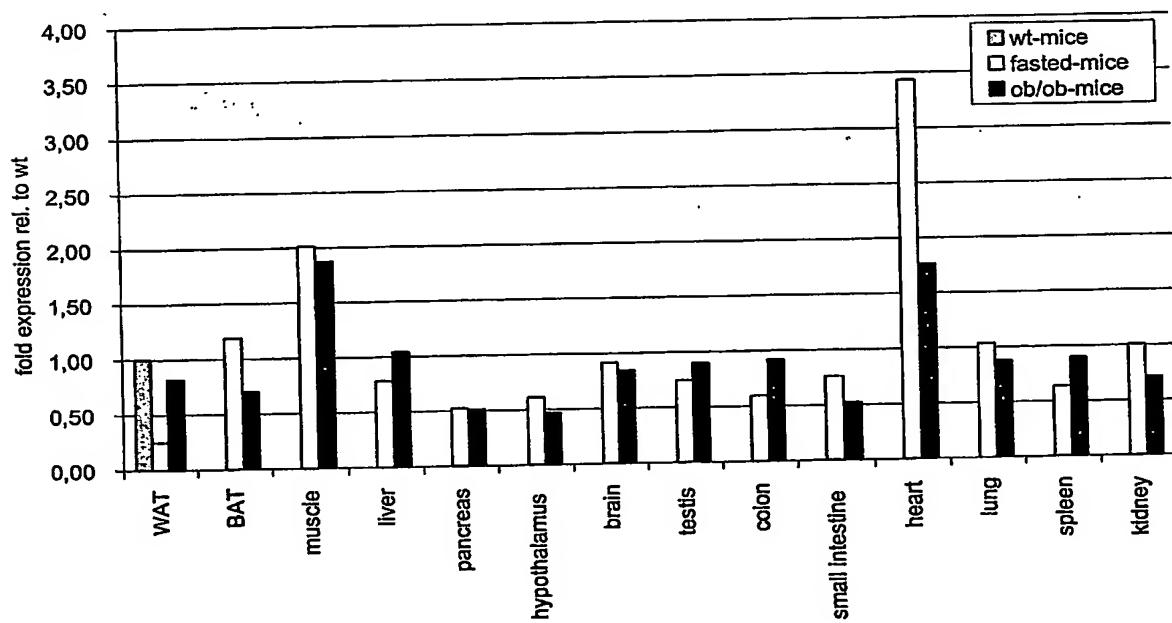
Figure 4. Expression of Prl-1 in different mammalian models**Figure 4A. Real-time PCR analysis of Prl-1 expression in wild type mouse tissues****Figure 4B. Real-time PCR analysis of Prl-1 expression in different mouse models**

Figure 4C. Real-time PCR analysis of Prl-1 expression in adipocytes during differentiation of 3T3-L1 cells from preadipocytes to mature adipocytes

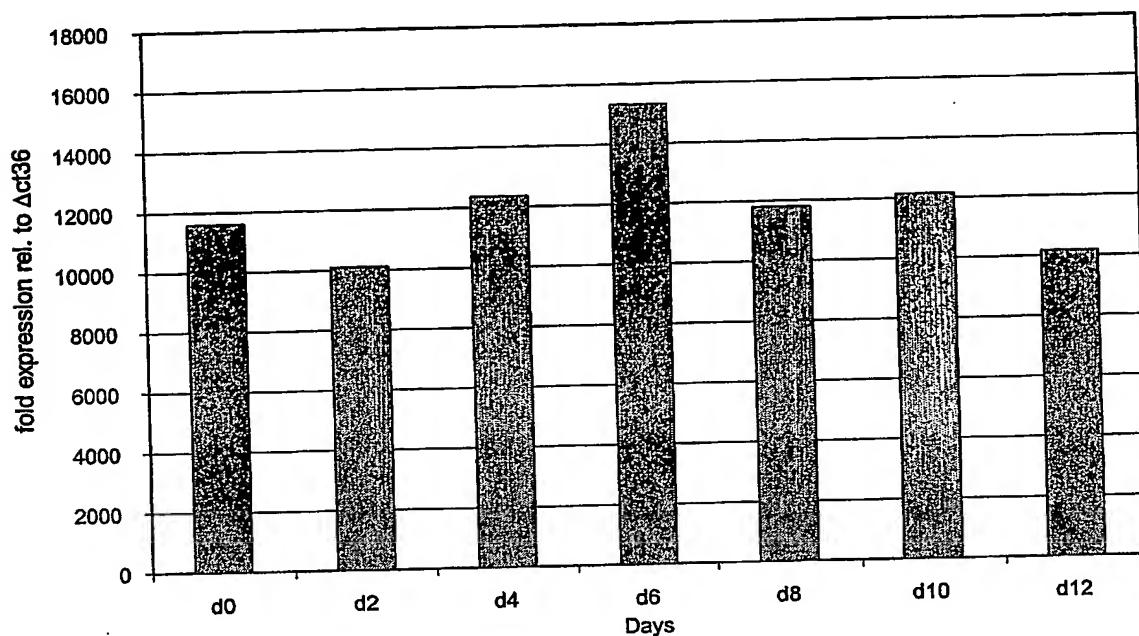


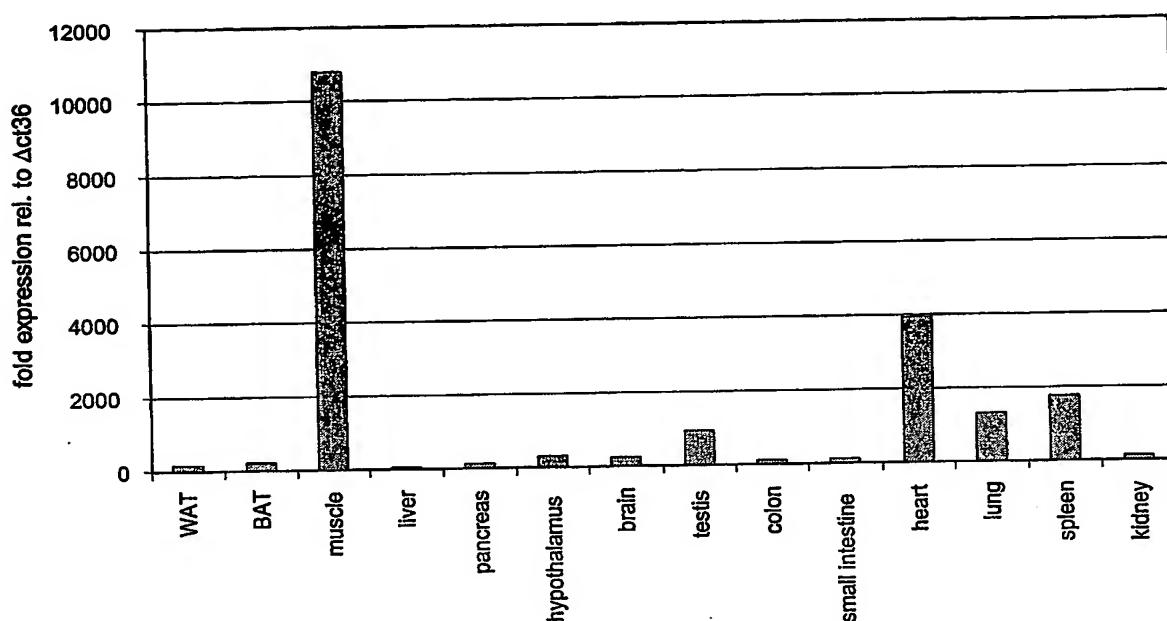
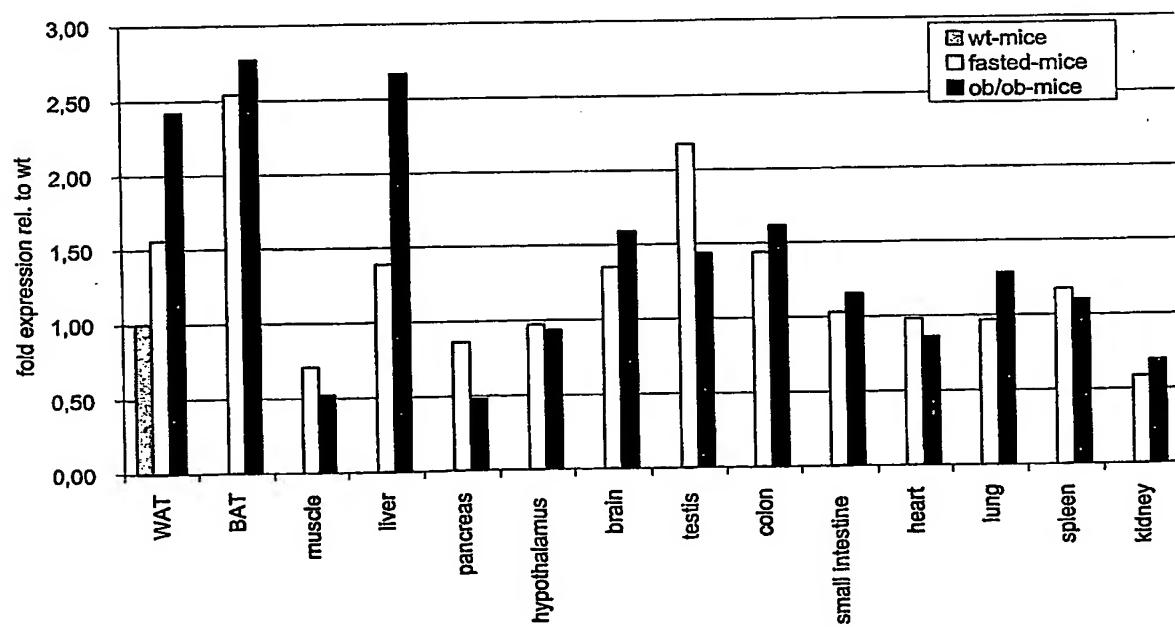
Figure 4D. Real-time PCR analysis of Prl-3 expression in wild type mouse tissues**Figure 4E. Real-time PCR analysis of Prl-3 expression in different mouse models**

Figure 4F. Real-time PCR analysis of Prl-3 expression in wild type mice fed a high fat diet compared to mice fed a control diet

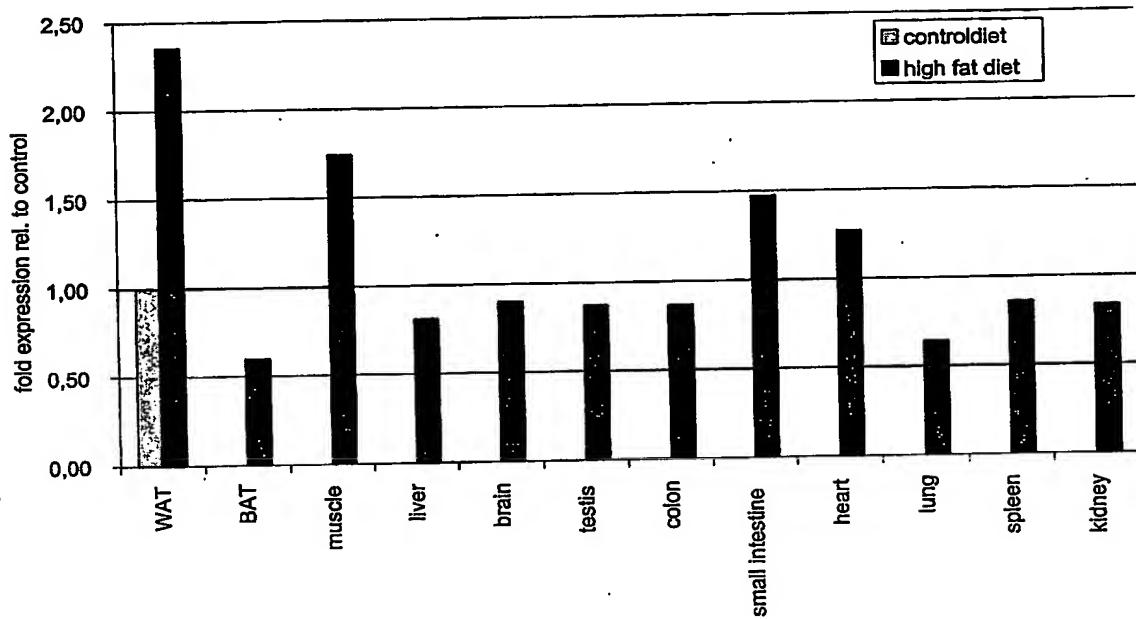


Figure 4G. Real-time PCR analysis of Prl-3 expression in adipocytes during differentiation of 3T3-L1 cells from preadipocytes to mature adipocytes

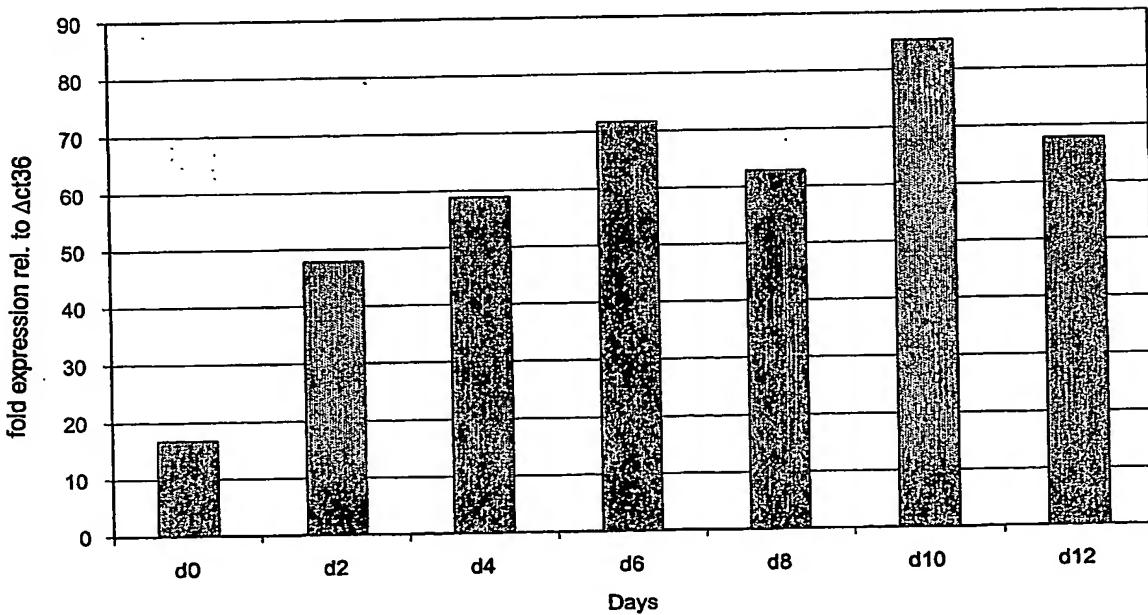


Figure 5. In vitro assays for determination of triglyceride storage and glycogen levels in adipocytes overexpressing Prl-1

Figure 5A. Up-regulation of cellular triglyceride levels in cells overexpressing Prl-1

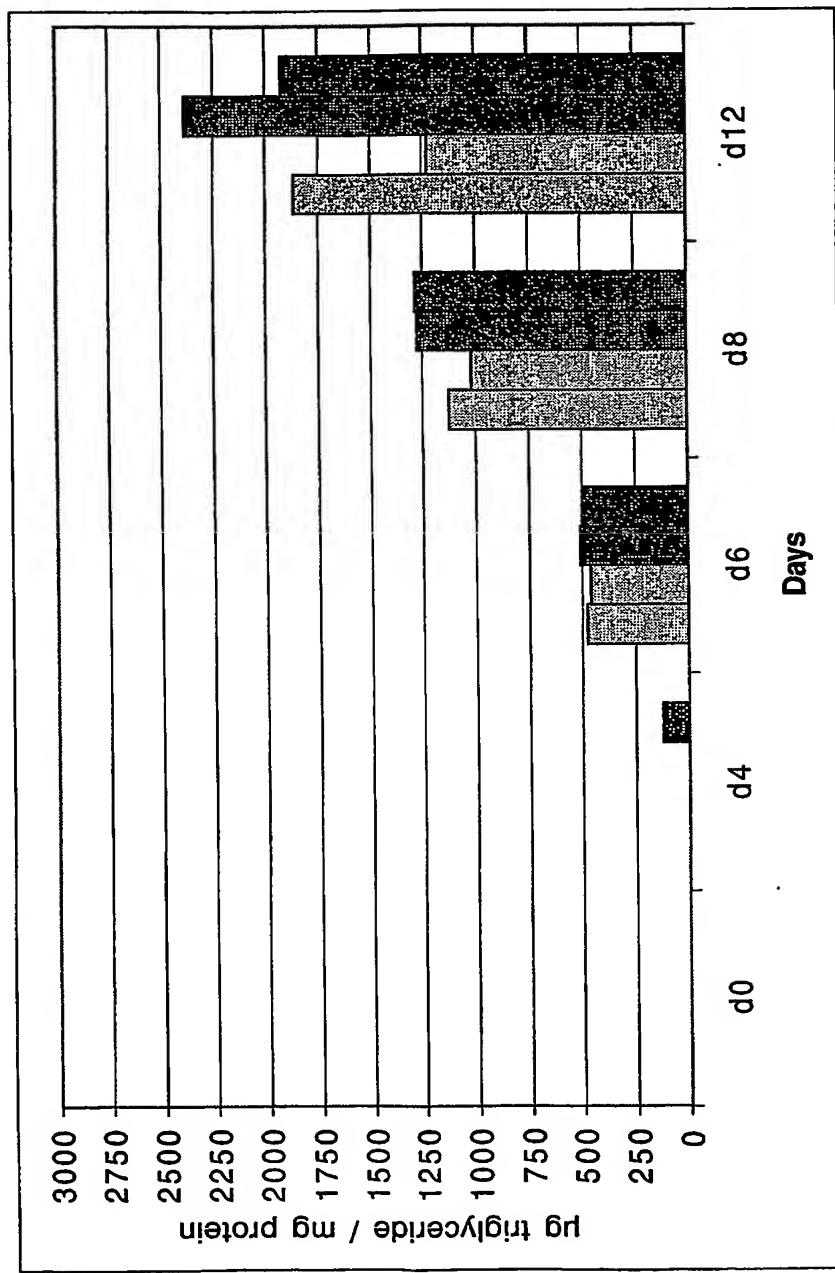


Figure 5B. Up-regulation of cellular glycogen levels in cells overexpressing Pr1-1

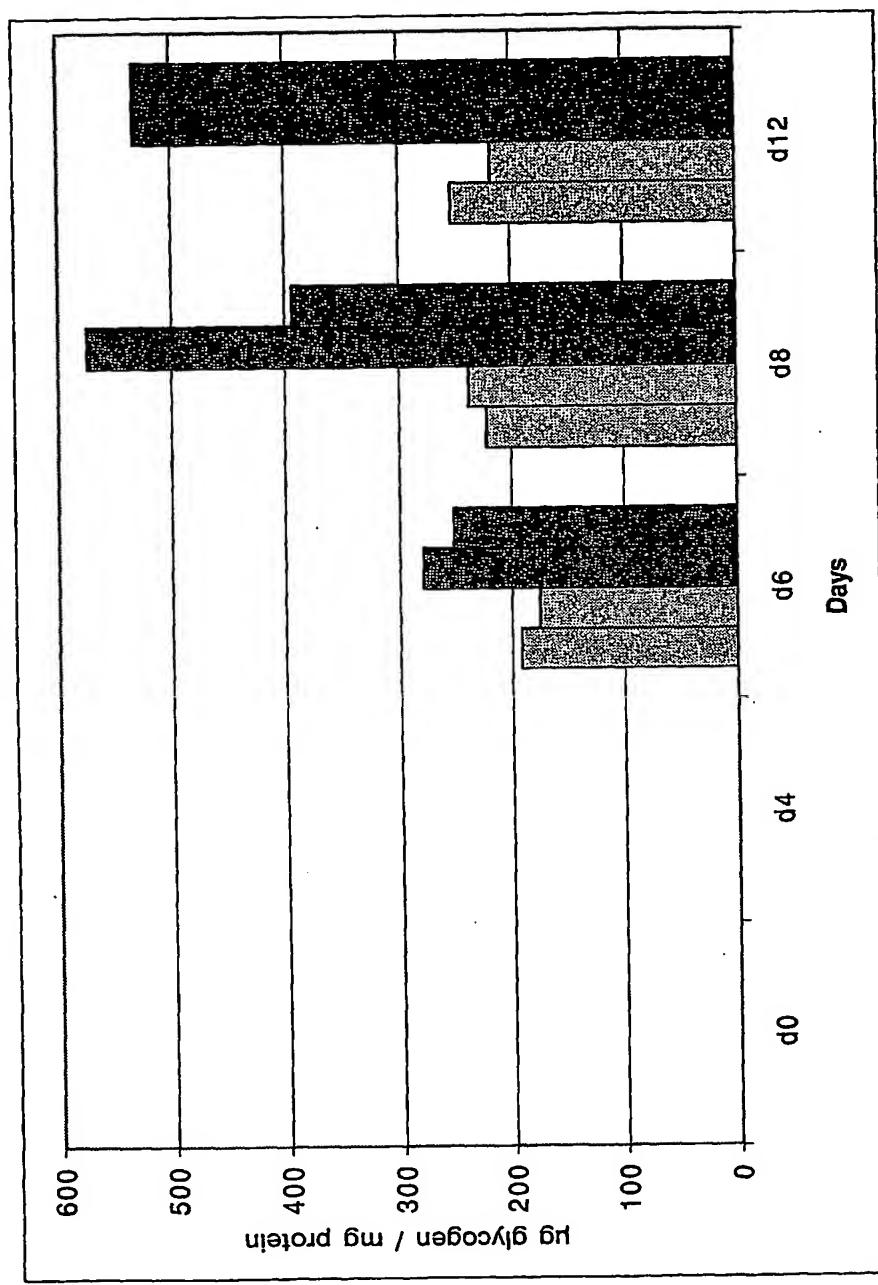


Figure 6. In vitro assays for determination of lipid synthesis and esterification of free fatty acids in Prl-1 loss of function (LOF) adipocytes

Figure 6A. Lipid synthesis levels on day 6 of differentiation in Prl-1 LOF 3T3-L1 cells

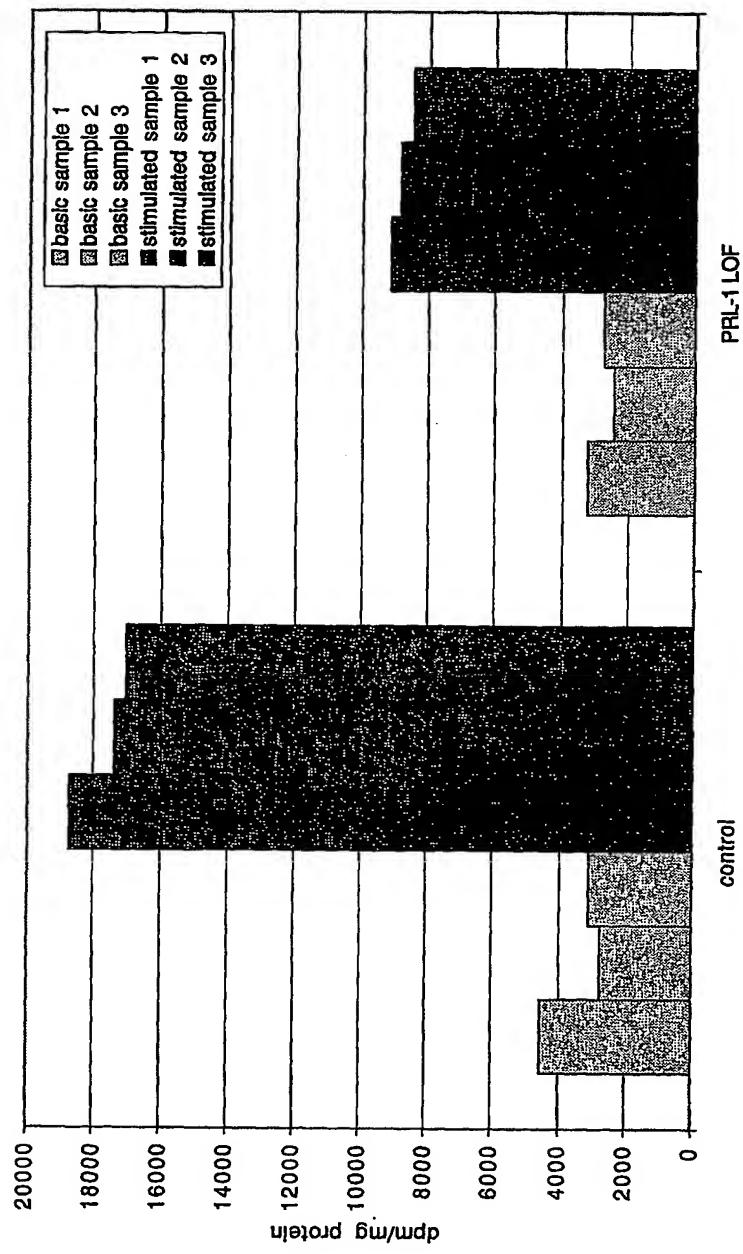


Figure 6B. Fatty acid esterification levels after free fatty acid uptake on day 12 of differentiation in Prl-1 LOF 3T3-L1 cells

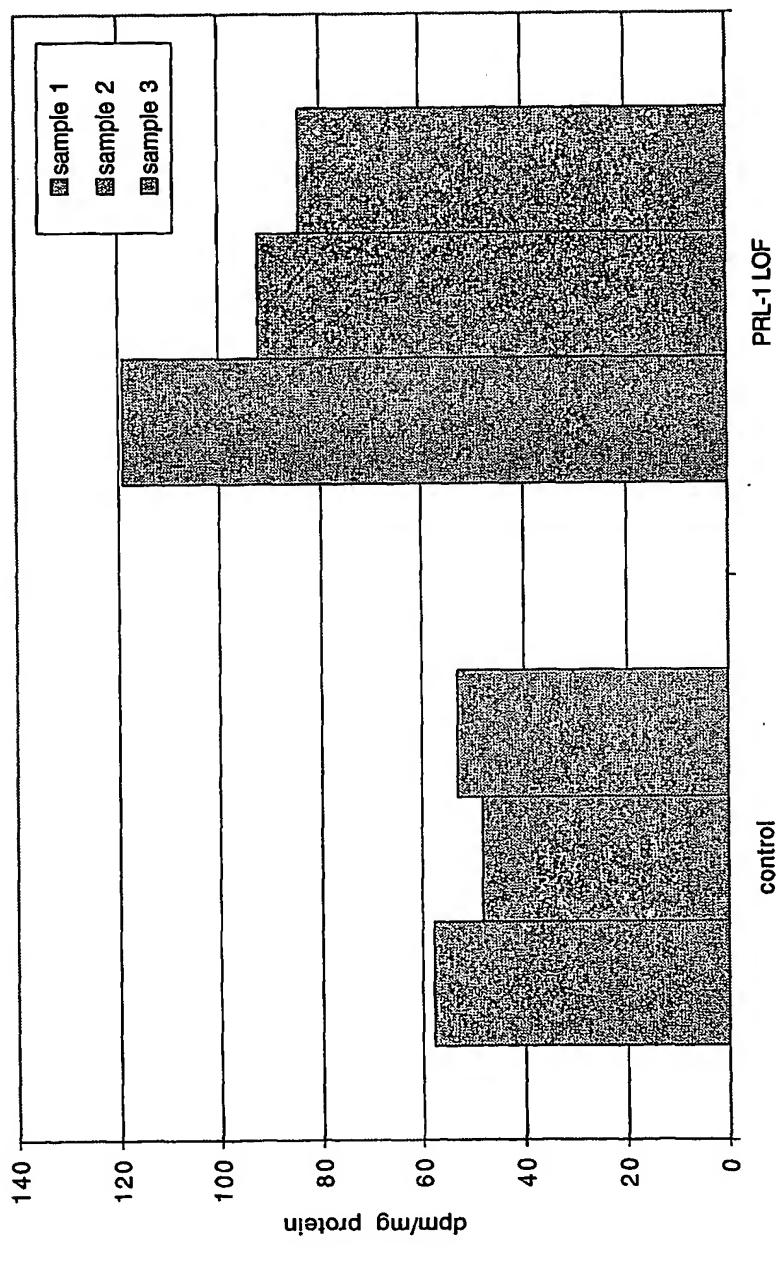


Figure 7. Expression of human *PRL-1* homologs in mammalian (human) tissue

Figure 7A. Microarray analysis of *PRL-1* expression in abdominal derived primary adipocyte cells during the differentiation from preadipocytes to mature adipocytes

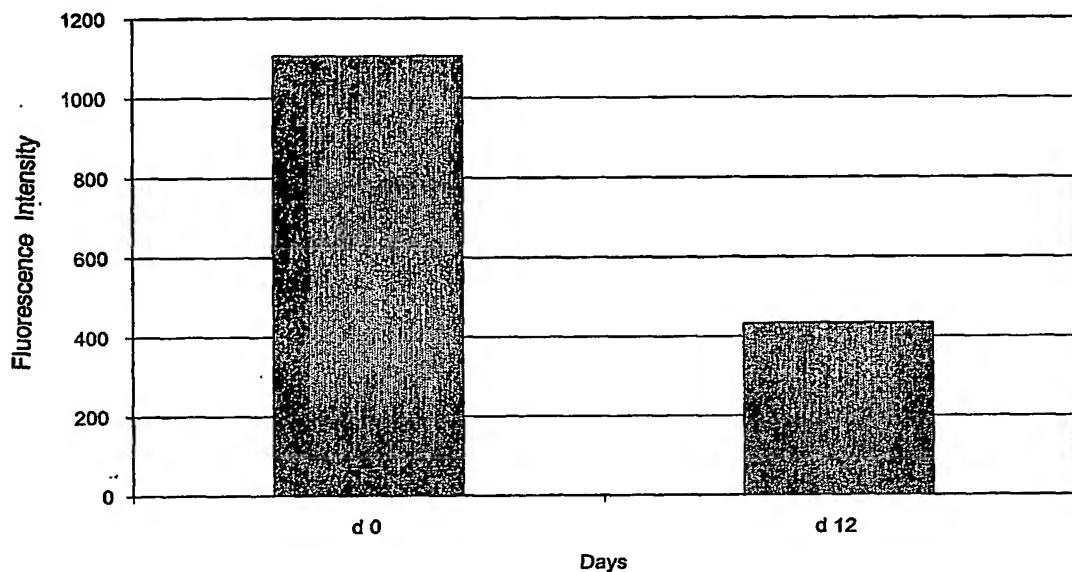


Figure 7B. Microarray analysis of *PRL-1* expression in a human adipocyte cell line during the differentiation from preadipocytes to mature adipocytes

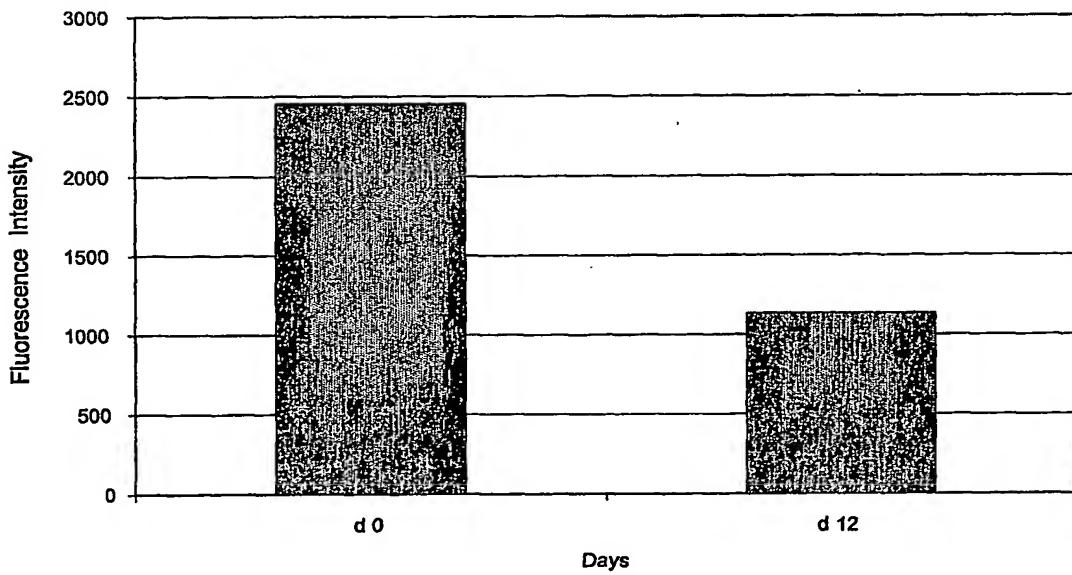


Figure 8. Real-time PCR analysis of the expression of *PRL-1* homologs in different human tissues

Figure 8A. Real-time PCR analysis of *PRL-1* expression in different human tissues

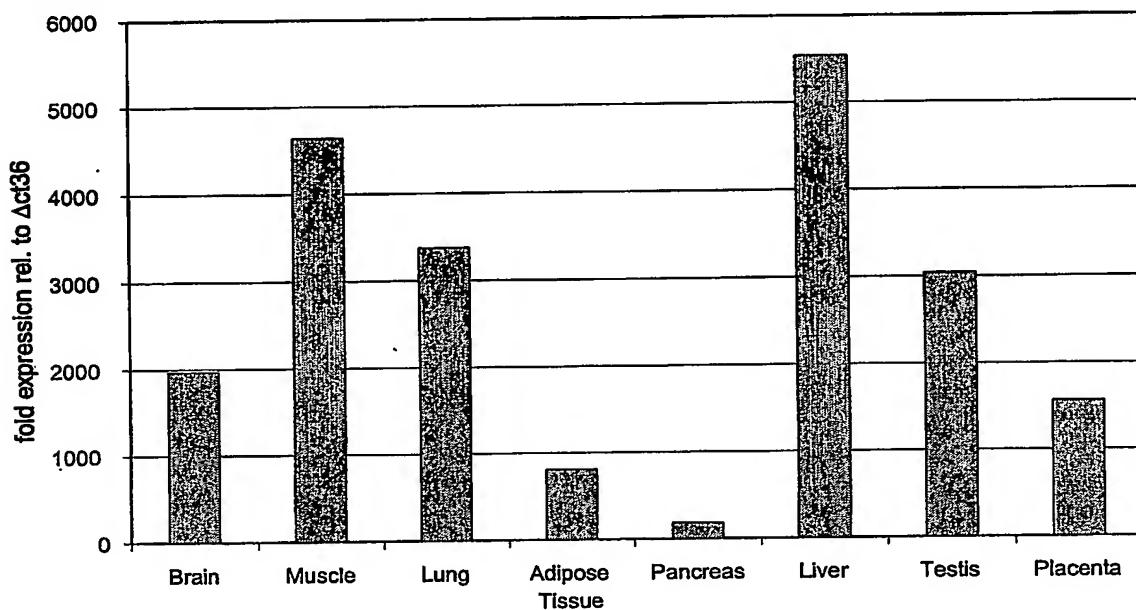
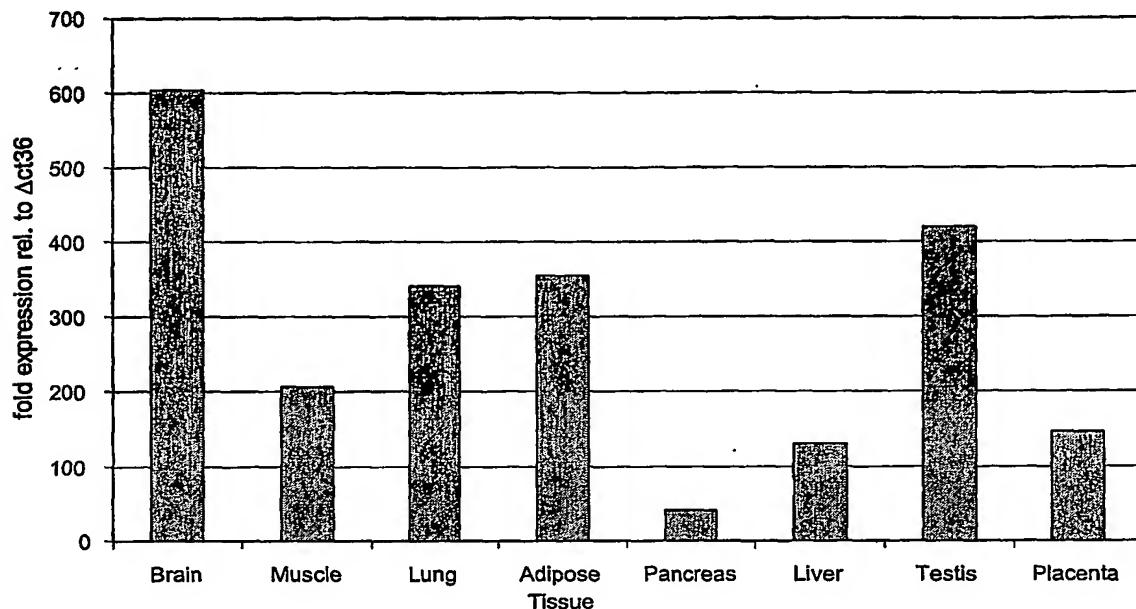
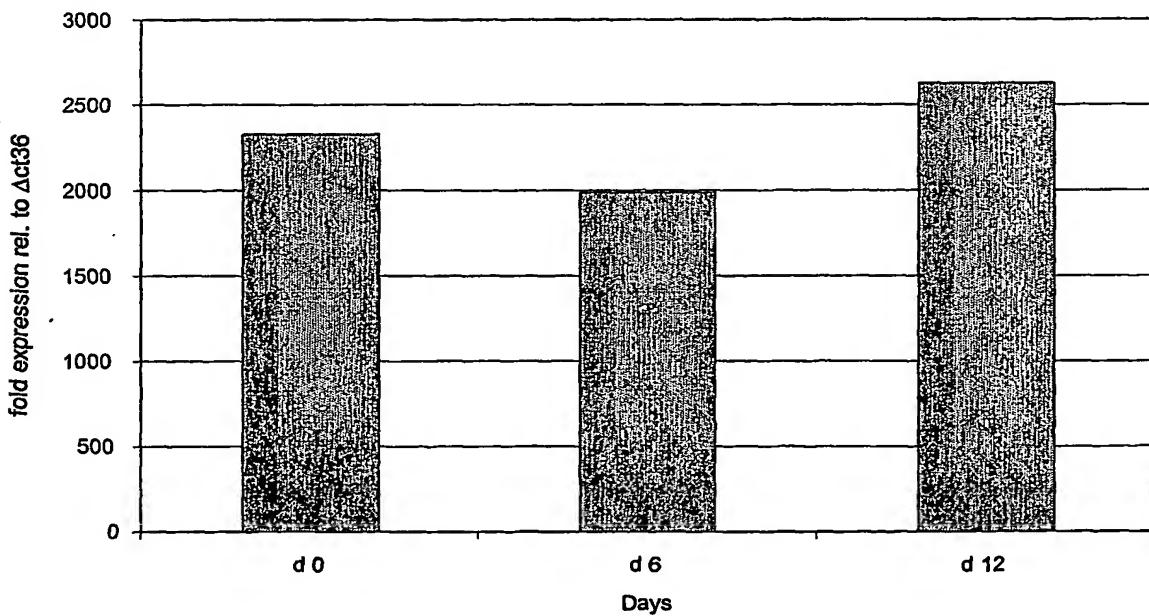


Figure 8B. Real-time PCR analysis of PRL-2 expression in different human tissues**Figure 8C. Real-time PCR analysis of PRL-2 expression in human primary adipocytes during preadipocyte differentiation**

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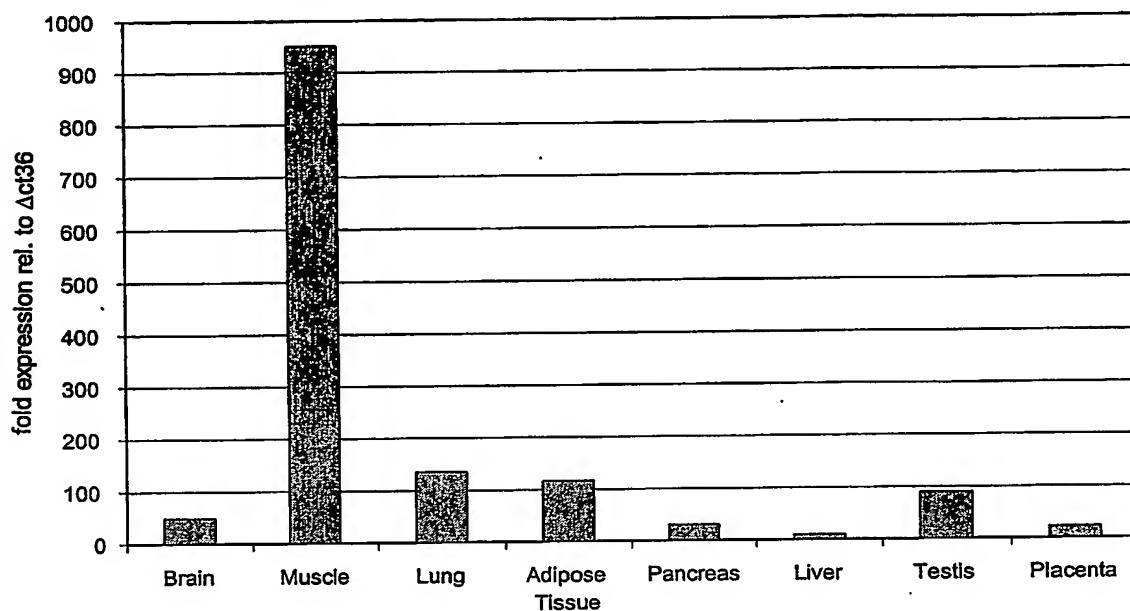
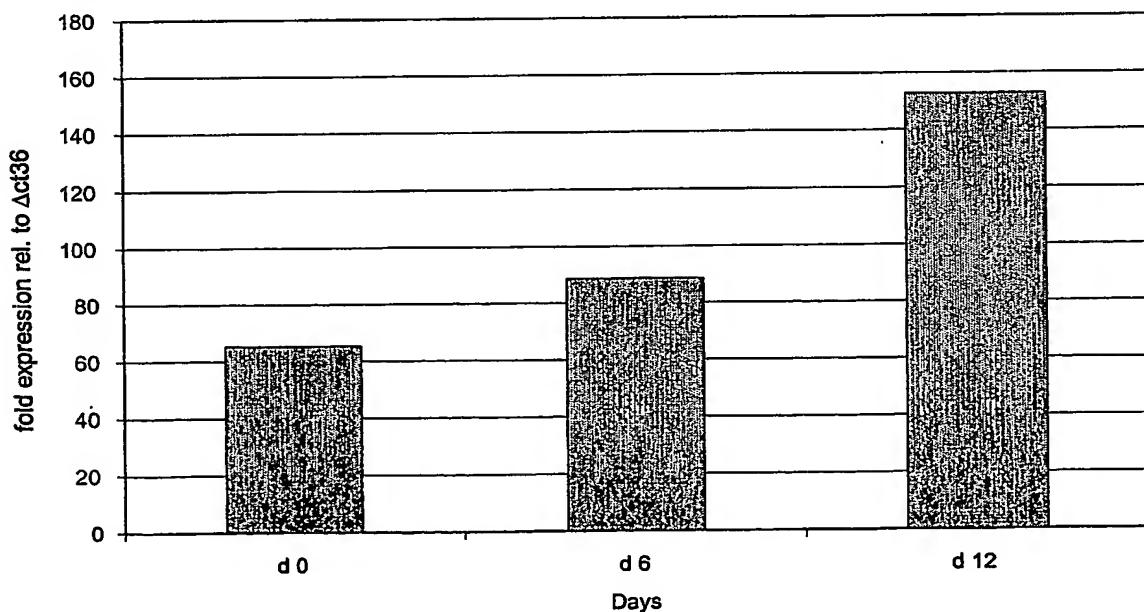
Figure 8D. Real-time PCR analysis of PRL-3 expression in different human tissues**Figure 8E. Real-time PCR analysis of PRL-3 expression in human primary adipocytes during preadipocyte differentiation**

Figure 9. In vitro assays for determination of free fatty acid and glucose uptake by adipocytes overexpressing Prl-1

Figure 9A. Up-regulation of free fatty acid uptake in SGBS cells overexpressing Prl-1

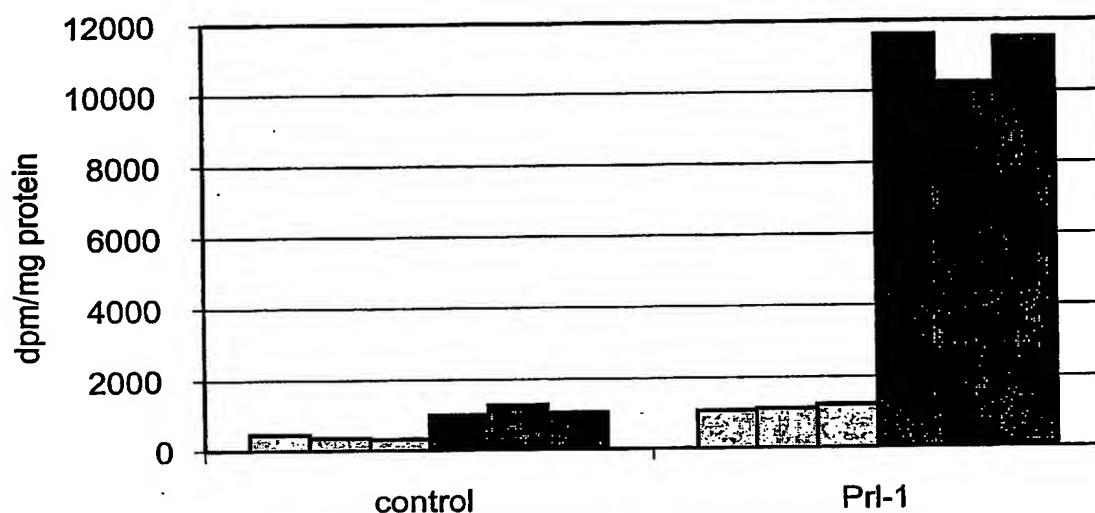


Figure 9B. Up-regulation of glucose uptake in SGBS cells overexpressing Prl-1

